



FINAL TECHNICAL REPORT

ONR Contract No. N00014-90-C-0035

PRINCIPAL INVESTIGATOR: Kenneth Buchi, M.D.
Richard Straight, Ph.D., Program Manager
Craig Taylor, Ph.D.

INSTITUTION: John A. Dixon Utah Laser Institute, University of Utah

PROGRAM TITLE: Medical/Materials Research and Applications of Free Electron Laser and Related Technologies

AWARD PERIOD: 3/1/88 - 3/31/91

OBJECTIVE: (1) To investigate biomedical and materials laser-optical systems that have potential clinical and industrial applications. (2) To develop clinical and industrial applications of Free-Electron laser technology and related broadly wavelength tunable, short pulse, ultrafast, high peak power, high average power laser systems that are efficient, compact, reliable and clinically and commercially practical systems. (3) To carry out actual FEL experiments with collaborators at existing FEL facilities at Duke, Vanderbilt and Stanford Universities.

APPROACH: The Program Objectives of the Utah MFEL Center are being pursued through a group of research and applications projects. The project titles are:

- (1) Tunable, pulsed laser photoion microscopy for mapping of biomolecule and DNA sequencing; an important new biomedical application of free electron laser technology. Requires development of optical systems for FEL harmonic generation, multiphoton activating, beam transport, pulse isolation, light delivery through optical fibers and IR and mass detection systems.
- (2) New possibilities of spectroscopy and selective photothermo therapy of spectrally and spatially heterogeneous tissue with tunable, ultrafast pulsed laser technology.
- (3) Temperature feedback control of FEL-induced thermal damage to targets.
- (4) Cancer diagnosis and treatment with targetable, light-activated polymeric drugs (photosensitizers).
- (5) Optical mammography: breast cancer imaging systems using ultrafast laser pulses.
- (6) Dental applications of lasers: improving caries resistance of dental enamel and VIS-IR surgical applications of lasers in dental health care.
- (7) Diagnostic and therapeutic applications of ultra fast laser spectroscopy of photochemical and photothermal photosensitizers for photodynamic therapy.
- (8) Hard and soft tissue surgical and photocoagulation applications of pulsed IR lasers.
- (9) Materials science projects to study disordered semiconductors and insulators, nonlinear and ultrafast processes and materials photochemical and photophysical processes.

Each project has a multidisciplinary research team assigned, made up of students, faculty and core MFEL staff. The MFEL program is guided scientifically and administratively by a steering committee consisting of

DISSEMINATION STATEMENT A
Approved for public release
Distribution Unlimited

19950925 104

Dr. Benner (Electrical Engineering); Dr. Buchi (Medicine); Dr. Straight (Laser Institute, Photobiology, Medicine and Surgery); Dr. Spikes (Biology); Dr. Taylor (Physics) and Dr. Wight (Chemistry). The steering committee meets regularly once a month or as needed. A separate committee of research project coordinators meets weekly to provide ongoing research direction.

ACCOMPLISHMENTS: The following is a summary of Program accomplishments. Accomplishments for each project are included also in separate publications.

1. Research Accomplishments (See list of Publications, Abstracts). The Program research accomplishments are presented for convenience in four categories although some of the work overlaps due to multidisciplinary research team approach. The categories are basic biomedical research, basic materials science research, clinical/industrial applications research and simulated and actual FEL research.

a. Basic biomedical research.

(1) Tunable, pulsed laser photoion microscopy for mapping and sequencing of biopolymers. We have developed the ultra fast picosecond and femtosecond laser-optical systems required for the project. The ultrafast laser system is to be completed soon. Earlier work on the Mark III FEL at Stanford on FEL harmonic generation tuning in the visible-IR range, beam transport and pulse isolation required for this project has been restarted at the Duke FEL (Mark III) facility by Ph.D. candidate Brett Hooper. The synthetic-polymer-dye work of Nancy Krinik under the direction of Dr. Kopecek, Dr. Spikes and Dr. Straight was originally undertaken as part of our work on drug delivery for photodynamic therapy but will be useful for this project also. The current work on PDT was most recently presented as SPIE, Biomedical Optics 92, Vol. 1645 and submitted for publication. It should be possible to use these synthetic polymer-dye systems as model compounds for studying the technical problems of polymer sequencing with pulsed laser-generated photoions.

(2) Ultrafast laser perturbation spectroscopy and selective photothermotherapy on a nanometer scale in spectrally and spatially heterogeneous tissue. Dr. Spikes (Professor of Biology) is one of the research coordinators of this effort. He has identified photosensitizers that efficiently convert light to heat and has determined radiative and nonradiative quantum yields for several dyes that may be useful for both spectroscopic applications and subcellular scale photothermal effects. We have previously published on the enhanced effectiveness of 20 ns pulsed (kHz), 628 nm light compared to CW light of the same average power on tumor tissue damage containing hematoporphyrin derivative photosensitizer. We still interpret these results as due to micrometer scale effects of nanosecond pulsed light. Picosecond and femtosecond pulses should make it possible to produce "selective" nanometer and subnanometer scale effects by the photothermal mechanism. The clinical importance of microscopic effects of pulsed light in tissue has already been demonstrated by the use of focused picosecond infrared (1064 nm) pulses for micrometer scale "explosive" ablation within the cornea by plasma formation.

Dr. Yoon has a manuscript in press (Applied Optics) on coherent backscattering (CB) in biological media for measurement and estimation of optical properties. A research team is studying potential direct applications in ophthalmology and dermatology. Work based on CB is proposed for separate funding to develop a simple, non-invasive, computer-controlled device for detecting early and residual cataracts for clinical use in ophthalmology. The ultimate goal of the proposed work is to design and construct a simple, non-invasive and computer-controlled device for diagnosing cataracts. A cataract is the development of opaque regions in the crystalline lens of the eye due to various causes, often associated with aging. A clinical examination is apt to be subjective and there have been no reliable methods to objectively quantify cataracts $\downarrow \uparrow \downarrow$. Aggregated biomolecules and inhomogeneities produce light scattering and the lens coloring from yellow to

brown is more related to absorption. The proposed optical method is based on coherent backscattering (CB) of light. CB is a recent development in random scattering theory. It occurs when light scatters through disordered biomolecules as a consequence of time reversal symmetry in the scattering paths. The phase enhancement is induced within about a few milliradian angular cone in the opposite direction of beam propagation. Usually, it is difficult to quantify both scattering and absorption from backscattering measurement only. However, the degrees of scattering and absorption can be measured from the magnitude and shape of the CB peaks. Radiative transfer theory used to describe light propagation in biological media does not explain this effect. A very accurate experimental setup for measuring CB is needed. During a one year period of investigation as a pilot project, a viability of CB in measuring absorption and scattering of the eye lens has been studied and correlations with various clinical stages of cataracts examined in order to quantify these cataracts. For the safety of the eyes, extremely low level of red light will be applied in clinical studies by using a highly sensitive charged-couple array as a detector whose quantum efficiency is over 50%. Experiments were performed in three steps, first with controlled media such as milk solutions to verify the proposed method, second with $\uparrow \downarrow$ eye samples, and finally $\uparrow \downarrow$ with New Zealand White rabbits. To our knowledge, no attempt has ever been made to quantify cataracts in terms of both lens scattering and absorption. If the pilot project in progress proves to be successful, it will lead to the development of a clinical diagnostic device which is simple and inexpensive, at the same time based on the novel physics of random light scattering.

(3) Temperature feedback control of FEL/pulsed laser-induced thermal damage to tissue. Dr. Yoon (Post-Doctoral Fellow) has completed a study on "Temperature rise during photodynamic therapy in a mouse tumor model," a comparison of pulsed vs CW light. The manuscript has been submitted for publication. Dr. Yoon developed theoretical models for temperature rise and feedback control systems and thermal camera-based detection system that can be readily transported to an FEL facility.

(4) Cancer diagnosis and treatment with a targetable light activated drugs (photosensitizers). Dr. Kopecek's project, "A polymeric drug delivery system for the simultaneous delivery of drugs activatable by enzymes and/or light," has been presented and published during the past year. Dr. Kopecek (Ph.D. student) successfully synthesized polymer drugs containing dark anticancer drugs and photosensitizers and demonstrated their effectiveness alone and combined in an animal tumor model. Merci Mader has just completed her research work, "Resistance to multiple chemotherapeutic agents in tumor cells: A possible solution using novel mechanisms of photochemotherapy." She developed a drug-resistant tumor cell line and then showed how tumor cells resistant to chemotherapy could be destroyed with light-activated photochemotherapy. She also made important contributions to understanding cellular-molecular mechanisms of drug resistance. The polymeric-drug delivery systems being studied as part of the MFEL program are very important for advancing the clinical use of PDT and are also important research tools as model compounds for pulsed laser photoion identification and biopolymer mapping. Dr. Straight has organized a symposium on polymer drug PDT at the invitation of the controlled Drug Release Society as part of their 19th International Congress on "Controlled Release of Bioactive Materials," July 26-31, 1992.

(5) Optical mammography: breast cancer imaging system using ultrafast laser pulses. This project is directed by Dr. Hebden, a Ph.D. physicist in the Department of Radiology. The ultimate goal of this project is to develop a clinical method of screening for breast cancer using clinically safe, non-ionizing, visible or near-infrared light. A device will ultimately be developed which is able to record and discriminate between the time-of-flight of photons that penetrate through the human breast, and which uses a fraction of the light with the shortest travel times to construct an image. The initial aim is to produce a device capable of achieving single

☒
☐
☐

Results

es

Dist	Avail and/or Special
A-1	

projection transmission images with a spatial resolution of a few millimeters or better. Dr. Hebden has made remarkable progress during the initial work period which has been published in six publications. He has also been awarded NIH and Whittaker Foundation funding to help support the project. Further advancement depends on work with the new ultrafast (femtosecond) laser-optical system in the core MFEL program.

(6) Dental applications of lasers. This project is coordinated by Dr. Lynn Powell (Professor of Dentistry). Dr. Powell has been very productive in studies on basic and clinical applications of lasers to dentistry. He has completed four publications on practical applications and has organized the 3rd International Congress on Lasers in Dentistry to be held in Salt Lake City, August 6-8, 1992.

(7) Diagnostic and therapeutic application of ultrafast laser spectroscopy of photochemical and photothermal photosensitizers for photodynamic therapy. This project is jointly coordinated by Dr. Benner, Dr. Buchi, Dr. Spikes and Dr. Straight. There have been nine publications and four abstracts published from work on this project. These have dealt with photophysical, photochemical, and photothermal properties of photosensitizers and $\uparrow\downarrow$ diagnostic fluorescence and Raman spectroscopy and imaging for cancer detection and treatment. Further work on this project will use the newly developed ultra fast laser-optical systems.

(8) Hard and soft tissue surgical and photocoagulation applications of pulsed IR-VIS laser systems. This work is jointly coordinated by Dr. Buchi, Dr. Bjorkman, Dr. Hunter, Dr. Taylor, and Dr. Straight. Most of the work on this project has been in the preclinical or clinical applications research category. Three abstracts have been published on endoscopic laser ablation of gastric and esophageal tissue abnormalities. One manuscript is submitted on endoscopic laser therapy of Watermelon stomach. This work of Dr. Buchi and Dr. Bjorkman represents basic studies to further develop minimally invasive endoscopic laser procedures. This is an area where laser technology is important, if not essential, and an area for new technology development.

Basic studies on light-tissue interaction have been completed with a new pulsed solid state infrared laser (Nd:YAG) wavelength of 1.44 μm which corresponds to a minor water absorption peak. This work is supported in part by Laserscope, Inc. The data were used to make clinical/commercial decisions for offering this wavelength on their existing 1.06/532 clinical laser systems. This is a high repetition rate pulsed laser for multiple clinical use. The solid state system has been highly successful and was developed and tested in collaboration with the Utah MFEL program. Dr. Mark Taylor in dermatology and Dr. Buchi in gastroenterology have found this system to be very effective.

b. Materials science basic research projects are summarized in four areas: (9.1) Disordered semiconduction; (9.2) Photochemical and photophysical processes; (9.3) Disordered insulators; and (9.4) Nonlinear and ultrafast processes. The research accomplishments are summarized in separate project reports. Studies on photochemical and photophysical processes and nonlinear and ultrafast processes strongly interact with several of the biomedical projects.

c. Clinical/industrial applications research.

(1) Clinical applications research. Two technical reports were written on the therapeutic application of new infrared, pulsed, ultrafast (PS) laser systems for microsurgery within the eye (e.g. intracorneal ablation for corneal reshaping to improve vision) for Storz Optical, Intelligent Surgical Lasers, Inc. and Phoenix Laser, Inc. The reports were used to make commercial decisions about developing a clinically approved, solid state, infrared laser-optical system (~\$280,000) for safe eye microsurgery as an alternative to excimer laser technology. The infrared system uses several DOD spin-off

technologies including infrared pulsed laser, optical guidance systems, and imaging systems to produce a very user-friendly, computer controlled clinical system to position, aim, fire, evaluate and refine, if necessary, to ablate a 10-20 μm target within a 50-100 μm zone (corneal thickness). This is an excellent example of a clinically and commercially important pulsed IR laser development from military systems spin-off. It has the potential of significantly improving health care, reducing overall health care costs and providing new jobs.

A technical report to be submitted for publication was written on studies of light-tissue interactions of the pulsed (Q-switched, ns) Nd:YAG IR wavelength 1.44 μm for surgical applications. The data were used to make a commercial decision about marketing this wavelength with FDA approval as part of an already very successful two wavelength (1064, 532) Nd:YAG frequency doubled clinical laser. The medical laser company, Laserscope, plans to market this wavelength but in a separate device.

Pulsed IR laser technology was evaluated in collaboration with Abbot Critical Care laboratories as a method for drilling micron diameter holes in heart catheters as a production process. This study is still in progress.

The portable, Raman based spectroscopic device for respiratory gas analyses for clinical use that was developed by a Utah start-up company (OHMRDA/ALBION) is a good example of our previous success in clinical technology development, transfer and commercialization that produces a small compact, low-cost clinical device useful in both civilian and military medicine. The process involved basic research (both biomedical and basic science); engineering; preclinical evaluation; cooperative research and development agreements; patent and technology licensing; new start-up companies; and successful clinical use and commercialization with the creation of new jobs. This is a long-term process of 5-10 years. We are still evaluating and testing potential new applications of the Raman based system.

The development of new clinical applications of light-activated drugs (HPD) used for cancer PDT in collaboration with Lederle Laboratories and the Canadian company, QLT, Inc. has led to a potential new PDT treatment for genital warts. We are evaluating several photosensitizer preparations and topical delivery methods and pulsed VIS-near IR lasers for clinical use. We have developed a rabbit papilloma virus wart model for these studies and have the only existing bank of wart material for research. We supply other investigators with this material (UCLA, Univ. Arkansas, Univ. British Columbia, University of Toledo, etc.).

Dr. Gellerman has developed several near-IR color center lasers with the potential of covering the wavelength range of 1 μm - 3 μm and capable of producing ultrafast pulses (fs-ns) as a FEL simulator. Dr. Gellerman has transferred this technology to Bell Laboratories under a cooperative research and development agreement.

(d) Simulated and actual FEL research. We have developed a new tunable, ultrafast (fs-ns) pulsed laser capability at a cost of nearly \$300,000 resulting from non-FEL sources that includes a new Nd:YAG amplified picosecond system; a Nd:YLF based, titanium-sapphire amplified femtosecond system and associated optical and detector components (see attached diagram and description). The system will be completely operational by October 1992. The Utah MFEL Center can then offer the most comprehensive ultrafast system available to other MFEL investigators and carry out many simulated FEL experiments including pump-probe experiments to study ultrafast processes in biology and materials science.

Brett Hooper (Ph.D. Candidate, Physics) is our expert on the Mark III FEL. He has been assigned to the Duke FEL Facility and has helped get that system operational again. He is an authorized Mark III operator. He has started up our earlier studies on FEL tunable frequency doubling, beam

transport, and optical fiber development for IR wavelength. The earlier work was published (Journal of Laser Application, Vol 1(3):49-58, 1989, and Nuclear Instruments and Methods in Research A296:797-803, 1990). In addition to our ongoing biomedical FEL research, Dr. Vardeny (Physics) has an approved and funded FEL project at Duke on the photophysical properties of optical polymers that will start Summer 1992. Dr. Taylor has an approved and funded (\$30,000) project at the Vanderbilt FEL Center. A graduate student or post-doctoral fellow will be assigned to that facility.

2. Clinical/Industrial Accomplishments. A clinical laser endoscopy facility is under construction at the Medical Center under the direction of Dr. Buchi. This facility will facilitate our preclinical and clinical studies for developing laser endoscopic devices for diagnosis and therapy. The facility is in addition to the existing general clinical laser facility under the direction of Dr. John Hunter, which is used as a shared clinical facility by general surgery, gastroenterology, urology, dermatology, OB-gyn, and other clinical services. It is also in addition to the cardiology-ultrasound laser facility under the direction of Dr. Ron Jenkins.

3. Education Accomplishments (Graduates, Post-Docs, Courses)

a. During the 1988-1991 period the program supported three biomedical Ph.D. candidates (Nancy Krinick (PDT Polymer Drugs), Merci Mader (PDT Drug Mechanisms) and Duncan Yu (Dentistry); two Physics Ph.D. candidates (Gary Kanner, Li Xiang) and three electrical engineering Ph.D. candidates (Martin Marshall, Steve Turcotte, Echard Reihlen). Two post-doctoral fellows were trained: (1) Gilwoon Yoon, from A.J. Welch's program at the University of Texas has taken a position in industry with Samsung Electronics of Korea to establish a medical laser research program for them and Gary Kanner will finish in September and take a position at Los Alamos National Laboratories in laser biochemistry/spectroscopy lab. We currently have three post-doctoral fellows--Kyra Moellmann, Matisse Schrenpel and David Drobek.

b. The Laser Institute educational coordinator, Dr. June Freedman, has conducted 10 national post-graduate clinical courses related to the clinical use of pulsed light in dermatology, gastroenterology, PDT and minimally invasive endoscopic laser surgery. These hands-on courses are taught by local and imported clinical faculty and are a very valuable resource to interface clinical users with newly developed laser technology with medical laser companies. This provides practical immediate feedback to industry about the clinical acceptability of new technology transfer and commercialization as well as a valuable clinical training tool. The courses, for example, have played an important role in the development of Laserscope's pulsed, frequency doubled YAG system, a highly successful clinical laser.

c. NIH Clinical Laser Workshop. "Biomedical Applications of Lasers," for NIH Program Managers and Scientific Review Administrators. Dr. Straight will participate in the Workshop on June 13-14, 1992, and the subsequent special study section for R438 R44 proposals. This is an important educational activity for developing new funding support for biomedical and clinical lasers photomedicine research. This addresses one of the goals of MFEL programs to stimulate other agency support.

4. Technology Transfer Accomplishments

a. New procedures for clinical use of PDT to treat topical lesions (e.g. genital warts)--Lederle Labs and QLT of Canada (in progress).

b. Technical evaluation of new ultrafast (PS) IR laser-imaging guidance system for ophthalmology microsurgery--Storz Optical, Inc. (American Cyanamid). Completed. This is an important clinical laser advancement. FDA trials are in progress now.

c. Basic research and technical evaluation of new solid state, pulsed (ns), YAG, IR frequency-doubled laser system for high power (10 watts average), reliable, fiber connected pumped dye laser system for PDT-Laserscope (in progress). This is an important advancement in laser technology for PDT and should help clinical use of PDT by replacing older, costly, unreliable argon-dye laser technology. The FDA must be convinced that pulsed laser is equivalent to CW laser.

d. Clinical research and technical evaluation of new pulsed Nd:YAG 1.44 μm laser for general surgery--Laserscope (completed). Data to be used for industry and FDA evaluation. Manuscript in preparation.

e. Basic research and new laser device development of CW and ultrafast (FS) pulsed color center laser technology. Excellent simulation of FEL near-mid IR characteristics--Bell Laboratories (in progress).

f. Testing and evaluation of existing Raman-based clinical spectrometer for detection and quantitation of respiratory gases and blood constituents--OHMEDA/ALBION (in progress).

g. FDA clinical laser device and application workshop. These workshops are sponsored in part by the American Society of Lasers in Medicine and Surgery (ASLMS). Dr. Straight, as past Vice President and now Chairman of the ASLMS Research Committee, has held one workshop at FDA and plans two more in 1992. From 30-40 FDA reviewers attend the course. The purpose is to provide FDA with expert training and advice about laser-tissue interactions and laser technology to help them better and more efficiently evaluate new laser technology and applications for industry. This is a very important part of the technology transfer and commercialization process of new laser technology and an important part of the MFEL mission. The expertise developed from the pioneering research work of the MFEL program makes it possible to keep FDA officials informed at the "cutting-edge" of new laser technology and clinical applications.

SIGNIFICANCE: The Utah MFEL Program has important and possibly unique aspects to contribute to achieving the overall goals of the Medical Free-Electron Laser program. The MFEL program is a DOD technology transfer or free-electron laser spin-off program with major emphasis on medical/clinical applications and an additional emphasis on materials/industrial applications. There is also a special interest in benefits to military medicine and to commercialization of new laser/optical technologies. Utah Laser Institute experience has shown that these programmatic goals can perhaps best be achieved with a closely integrated, multidisciplinary, investigator-initiated collaboration among basic scientists, engineering scientists and clinical scientists. The Utah MFEL Center program has a cost effective mechanism through the John A. Dixon Laser Institute to establish the necessary investigator collaborations among existing academic faculty from basic science, engineering and clinical departments. The Laser Institute provides a relatively inexpensive core support staff and shared core facilities that maximizes the formation of multidisciplinary research teams, usage of major equipment and research grant funds. The broad participation of many university academic departments generates strong support from the University for programs such as the MFEL program. This support manifests itself in access to space, funding for major equipment, faculty salary support, technology transfer and patent support, administrative support and undergraduate, graduate and post-doctoral fellow support. Another important aspect is the broad range of clinical medicine and surgery subspecialties with established programs at Utah in laser photomedicine and the nationally recognized post-graduate clinical laser education program with courses offered throughout the year. The clinical areas with laser programs are general surgery, gastroenterology, urology, dermatology, ophthalmology, neurology, obstetrics/gynecology, pulmonary, oncology, nursing, pathological and dentistry. Regular laser medicine courses are taught in gastroenterology, dermatology, nursing and general surgery. Special courses are offered in

urology, oncology, dentistry and other specialties as needed. The courses are sponsored in part by medical laser companies and attended by physicians, health care workers and industry workers primarily from the United States and Canada but also from Europe, Asia and Russia.

These important assets have made it possible to identify relevant and important clinical problems that may be solved or facilitated through laser photomedicine and especially through tunable, pulsed, high peak power laser technology that can be developed through simulated and actual free-electron laser experiments. The Utah program is organized to identify significant, practical clinical and industrial needs that lend themselves to photo-optical solutions; to support basic materials and biomedical research relevant to the identified problems; to form multidisciplinary research teams to guide the research; to develop preclinical systems and approaches to the problems; to identify commercial sponsors for clinical/industrial device development and commercial use and to provide clinical/industrial post-graduate education for acceptance and advancement of new technology.

PUBLICATIONS AND ABSTRACTS

1. Tunable, pulsed laser photoion microscopy for mapping of biomolecule and DNA sequencing; an important new biomedical application of free electron laser technology. Requires development of optical systems for FEL harmonic generation, beam transport, pulse isolation, light delivery through optical fibers and IR and mass detection systems.
 - a. Hooper, B.A., Benson, S.V., Straight, R.C., Madey, J.M.J. (1990) Applications of harmonic generation of picosecond pulses from a free electron laser. Nuclear Instruments and Methods in Physics Research A1296: 797-803.
2. New possibilities of spectroscopy and selective photothermal therapy of spectrally and spatially heterogeneous tissue with tunable, ultrafast pulsed laser technology.
 - a. Straight, R.C., Benner, R.E., McClane, G., P.M.N.Y.H., Yoon, G., Dixon, J.A. (1991) Application of charge-coupled device technology for measurement of laser light and fluorescence distribution in tumors for photodynamic therapy. Photochem. Photobiol. 53: 787-796.
 - b. Yoon, G., Ghosh Roy, D.N., Benner, R.E., Straight, R.C. (1992) Coherent backscattering in biological media: measurement and estimation of optical properties. Applied Optics (In press).
 - c. Yoon, G., Sun, Y., Straight, R.C., Welch, A.J. (1992) Temperature rise during photodynamic therapy in a mouse tumor model. Submitted to Lasers in Medicine and Surgery.
 - d. Benner, R.E., McClane, R.W., Dixon, J.A., Straight, R.C. (1991) Light distributions from diffusing optical fiber tips. Lasers in the Life Sciences 4: 103-113.
 - e. Benner, R.E., McClane, R.W., Dixon, J.A., Straight, R.C. (1991) Light distributions from diffusing optical fiber tips. Lasers in the Life Sciences 4(2): 103-113.
 - f. Spikes, J.D. (1990) New trends in photobiology (invited review). Chlorins as photosensitizers in biology and medicine. J. Photochem. Photobiol. B. 6: 259-274.
 - g. Jori, G., Spikes, J.D. (1990) Photothermal sensitizers: possible use in tumor therapy. J. Photochem. Photobiol. B. 6: 93-101.
 - h. Spikes, J.D. (1988) Photochemotherapy: molecular and cellular processes involved. SPIE 997: 92-100.
 - i. Spikes, J.D. (1992) Quantum yields and kinetics of the photobleaching of hematoporphyrin, photofrin II, tetra(4-sulfonatophenyl)-porphine and uroporphyrin. Photochem. Photobiol. 60: 1-12.
3. Temperature feedback control of FEL-induced thermal damage to targets.
4. Cancer diagnosis and treatment with targetable, light-activated polymeric drugs (photosensitizers).
 - a. Kreger, D., Peterson, C.M., Jones, K.P., Poulson, A.M., Jolles, C.J., Straight, R.C. (1992) Photodynamic therapy of human endometrial carcinoma (HEC-1-A) heterotransplanted in nude mice. Abstract presented February 1992, Society for Gynecologic Investigation.

- b. Krinick, N.D., Sun, Y., Joyner, D., Reed, R., Spikes, J.D., Straight, R.C., Kopecek, J. (1992) A polymeric drug delivery system for the simultaneous delivery of drugs activatable by enzymes and/or light. Submitted to J. Controlled Drug Release.
 - c. Peterson, C.M., Reed, R., Jolles, C.J., Jones, K.P., Straight, R.C., Poulson, A.M. (1992) Photodynamic therapy of human ovarian epithelial carcinoma, OVCAR-3, heterotransplanted in the nude mouse. Submitted to Am. J. Obstet. Gynecol.
 - d. Winn, P., Buchi, K.N., Claerhaut, A., Straight, R.C. (1991) Photodynamic therapy in a human colon cancer model: continuous wave argon/dye laser versus pulsed wave gold vapor laser. Abstract presented May 10, 1991, American Society for Laser Medicine and Surgery Abstracts, 11(3): 28.
 - e. Bjorkman, D.J., Samowitz, W.S., Peterson, B.J., Straight, R.C. (1991) Fluorescence localization of early colonic cancer in the rat by hematoporphyrin derivative. Lasers Surg. Med. 11: 263-270.
 - f. Bjorkman, D., Samowitz, W., Peterson, B., Brigham, E., Straight, R. (1990) Photofrin II detection of early colonic cancer in the rat. Abstract presented May 10, 1990, Lasers Surg. Med., p 26.
 - g. Bjorkman, D.J., Peterson, B.J., Brigham, E.J., Samowitz, W.S., Straight, R.C. (1992) Efficacy of hematoporphyrin derivative in the detection of early colonic cancer in the rat. Gastroenterology 98: A46.
 - h. Straight, R.C., Go, P.M.N.Y.H., Benner, R.E., Dixon, J.A., McClane, R.W. (1990) Optical-CCD system for imaging light and drug distributions in tumors for phototherapy. SPIE Institutes for Advanced Optical Technologies IS6: 272-281.
5. Optical mammography: breast cancer imaging systems using ultrafast laser pulses.
 - a. Hebden, C., Kruger, R.A. (1990) Simulating the performance of a time-of-flight transillumination imaging system. SPIE Proc. Bioimaging and Two-Dimensional Spectroscopy 1205: 142-149.
 - b. Hebden, J.C., Reinecke, D.R., Kruger, R.A. (1989) Examining the feasibility of laser collimated transillumination. Medical Imaging III. SPIE Proc. 1090: 35-41.
 - c. Hebden, J.C., Kruger, R.A. (1990) Transillumination imaging performance: spatial resolution simulation studies. Med. Phys. 17: 41.
 - d. Hebden, J.C., Kruger, R.A. (1990) Transillumination imaging performance: a time-of-flight imaging system. Med. Phys. 17: 351.
 - e. Hebden, C., Kruger, R.A. Time resolved imaging through a highly scattered medium. Appl. Opt. 30 (in press).
 - f. Hebden, J.C. Evaluating the spatial resolution performance of a time-of-flight optical imaging system. Med. Phys. (Submitted).
6. Dental applications of lasers: improving caries resistance of dental enamel and VIS-IR surgical applications of lasers in dental health care.
 - a. Powell, G.L., Whisenant, B.K. (1991) Comparison of three lasers for dental instrument sterilization. Lasers Surg. Med. 11: 69-71.

- b. Blankenau, R.J., Kelsey, W.P., Powell, G.L., Shearer, G.O., Barkmeier, W.W., Cavel, W.T. (1991) Degree of composite resin polymerization with visible light and argon laser. *American Journal of Dentistry* 4: 40-42.
 - c. Powell, G.L., Whisenant, B.K., Morton, T.H. (1990) Carbon dioxide laser oral safety parameters for teeth. *Lasers Surg. Med.* 10: 389-392.
 - d. Wong, J., Otsuka, M., Higuchi, W.I., Powell, G.L. (1990) Effect of laser irradiation on the dissolution kinetics of hydroxyapatite preparations. *J. Pharm. Sci.* 79: 510-515.
7. Diagnostic and therapeutic applications of ultra fast laser spectroscopy of photochemical and photothermal photosensitizers for photodynamic therapy.
 - a. Spikes, J.D. (1991) Photophysical and photosensitizing properties of phthalocyanines. *Photobiology* pp 831-837.
 - b. Spikes, J.D., Bommer, J.C. (1991) 5.4 Chlorophyll and related pigments as photosensitizers in biology and medicine. In: Scheer, H., ed. *Chlorophylls*, CRC Press, Boca Raton, pp 1181-1204.
8. Hard and soft tissue surgical and photocoagulation applications of pulsed IR lasers.
 - a. Johnson, T.D., Markowitz, N., Berenson, M.M., Buchi, K.N. (1991) Argon laser photoablation of esophageal columnar epithelium combined with gastric acid suppression restores normal esophageal mucosa. Abstract presented May 10, 1991, American Society for Laser Medicine and Surgery Abstracts 11(3): 26.
 - b. Bjorkman, D.J., Buchi, K.N. (1991) Endoscopic laser therapy of the watermelon stomach, argon vs Nd-YAG. Abstract presented May 10, 1991, American Society for Laser Medicine and Surgery Abstracts 11(3): 26.
 - c. Bjorkman, D.J., Buchi, K.N. (1991) Endoscopic laser therapy of the watermelon stomach. *Clinical Research* 39: 5A.
 - c. Bjorkman, D.J., Buchi, K.N. (1992) Endoscopic laser therapy of the Watermelon stomach. Submitted to *Lasers Surg. Med.*
 - d. Taylor, M.B. (1991) Chondrodermatitis nodularis chronica helioides. Successful treatment with the carbon dioxide laser. *J. Dermatol. Surg. Oncol.* 17: 862-864.
 - e. Taylor, M.B. (1991) Flashlamp laser treatment of port wine stain hemangiomas and other vascular lesions using a defocused "fuzzy spot". American Society for Laser Medicine and Surgery Abstracts Suppl 3: 68.
 - f. Taylor, M.B. (1992) Use of multiple lasers for the treatment of vascular lesions in children and adults. American Society for Laser Medicine and Surgery Abstracts Suppl 4: 68.
 - g. Taylor, M.B. (1991) Treatment of acne vulgaris. Guidelines for primary care physicians. *Acne* 89: 40-47.
9. Materials science projects to study disordered semiconductors and insulators, nonlinear and ultrafast processes and materials photochemical and photophysical processes.

- a. Soccolich, E.E., Möllmann, K., Gellermann, W., German, K.R., Passively modelocked femtosecond color center lasers in the erbium gain band. Submitted to Appl. Phys. Letts.
- b. Schrempel, M., Gellerman, W., Luty, F. (1992) Persistent vibrational spectral hole burning and dephasing properties of orientationally aligned CN^- defects in cesium halide crystals. Physical Review B. 45: 28-39
- c. Möllmann, K., Mitschke, F., Gellermann, W. (1991) Optical properties and synchronously pumped mode-locked 1.73-2.10 μm tunable laser operation of $(\text{F}_2^+)_{\text{AH}}$ centers in $\text{KCl}:\text{Na}^+:\text{O}_2^-$ crystals. Optics Communications 83: 177-184.
- d. Gellermann, W. (1991) Color center lasers. J. Phys. Chem. Solids 52: 249-297.

DIXON LASER INSTITUTE RESOURCES

CLINICAL LASERS

Argon Lasers

- HGM Argon 8 Laser
- HGM Argon 20 Laser
- HGM Argon Laser (Ophthalmology)
- Coherent Argon Laser

CO₂ Lasers

- NIIC CO₂ Laser
- Illumina CO₂ Laser
- Sharpland Model 1020 CO₂ Laser

Dye Lasers

- Candela Flash-Pumped Dye Laser
- LaserSonics Aurora/M Argon-pumped Medical Dye Laser

Krypton Laser

- HGM Krypton Laser

Nd:YAG Lasers

- Model 8000 Nd:YAG Laser
- Cooper Vision Nd:YAG Laser

RESEARCH LASERS

Argon Lasers

- Spectra-Physics Model 2045; 25 W visible, 4.5 W ultraviolet
- Spectra-Physics Model 2060; 7 W visible, BeamLoc system
- Coherent INNOVA-90; 8 W, all lines
- Coherent INNOVA-90; 8 W, single mode
- American Laser Corporation Medical Argon Laser
- Spectra-Physics Model 171 20 W Argon Laser
- Several additional Argon lasers, 4 W
- Spectra-Physics Model 165-09 Argon Laser, 5 W

CO₂ Lasers

- Cavitron Model AO 300 CO₂ Microsurgery Laser
- Cavitron CO₂ Microsurgery Laser
- CO₂ Pulsed Laser
- Tachisto TEA CO₂ Laser

Color Center Laser

- KCl:Ti Laser; 1.4-1.6mm tunable, cw, 1W, (Optional Mode Locking)
- NaCl:(F₂⁺)_H Laser; 1.4-1.75mm tunable, cw, 2W, Mode Lock Option
- KCl:Na⁺:O₂- Laser; 1.7-2.1mm tunable, cw, 0.3W, Mode Lock Option

Copper Vapor Laser

- Metal-Laser Technologies Inc., Cu-Vapor Laser (Med. Center)
- Metal-Laser Technologies Inc. Cu Laser
- CVL/CPM optical amplifier (Physics)

CPM Laser

- CPM (Colliding-Pulsed-Modelocked) Laser

Dye Lasers

- Coherent Model CR-599 Scanning, Single-frequency Dye Laser
- Coherent Model 700 Synchronously-pumped Dye Laser (2)
 - cavity dumper
 - dye circulators
 - auto-correlators (2)
- Cooper Argon-pumped Medical Dye Laser (V.A. Hospital)

Molelectron DL-II Tunable Dye Laser
 Phase-R DL Series Flashlamp-pumped Dye Laser (3)
 Quantel International TDL50 Nd:YAG-pumped Dye Laser
 Quantel International PTL10 picosecond Tunable Dye Laser
 Lumonics Model EPD-20 Dye Laser
Excimer-Dye Lasers
 1-Physics Excimer/Dye Laser
 Questeck Model 2200 Excimer Laser, 200 mJ/pulse, 50Hz rep.
 rate
F-Center Lasers
 Burleigh Instruments Laser [

- Multimode System
- Single mode System

Gold Vapor Laser
 GVL Plasma-Kinetics Laser, 3 W 627.8nm (V.A. Hospital)
Helium-Cadmium Laser
 LiConix Model 4050 HeCd Laser
Helium-Neon Lasers
 Melles Griot HeNe Lasers (2)
 Spectra-Physics Stabilite Model 124B HeNe Laser
 Spectra-Physics Model 138 HeNe Laser
 50 mW HeNe Laser
 20 mW HeNe Laser
 Several smaller HeNe Lasers
Krypton Laser
 Spectra-Physics Model 3000 Kr Laser
Nitrogen Laser
 Nitrogen - Pumped Dye Laser
Titanium-Sapphire Lasers
 Spectra-Physics Model 3900 Ti-Sapphire Laser
 Clark Instruments Mode-Locked Ti-Sapphire Laser
Nd:YAG Lasers
 LaserSonics Model 8000 Nd:YAG medical Laser
 Quantel International Nd:YAG Laser
 Quantronix Model 416 Nd:YAG Laser

- mode-locked
- 2nd harmonic generator

 Quantronix Nd:YAG Laser
 Er:YAG Laser
 Ho:YAG Laser
 Nd:YAG Laser
 Er:YSGG Laser

}	Schwartz Electro-Optics 1-2-3 Laser - Q-switch Motor Speed Controller Accessory
---	--

OTHER EQUIPMENT RESOURCES

Spectrometers

Jarrell Ash 0.25m, f/6, single-stage spectrometer
 Spex 0.25m spectrometer
 Spex 0.3m, subtractive dispersion, double spectrometer
 Spex 1870, 0.5m, f/10, single-stage spectrometer with digital
 control interface.
 Spex 1870, 0.5m, f/10, single-stage spectrometer with minidrive.
 Bausch & Lomb gratings (50x50 mm); 0.5, 0.75, 1.25, 2.0 mm
 blaze
 Spex 500m, 0.5m, f/4, single-stage spectrometer with digital
 control interface.
 Bausch & Lomb gratings (110x110 mm); 1.0, 3.0, 8.0 mm blaze
 wavelengths

Spex 1877, 0.6m, triple spectrograph; subtractive dispersion double w/single
 Spex gratings; 300 gr/mm (3), 600 gr/mm (3), 1200 gr/mm (3)
 Spex 1403, 0.85m, double-scanning monochromator
 Spex gratings (110x110 mm); 1800 gr/mm holographic
 - Accessory 3rd monochromator
 - Microscope accessory for micro-probe measurements
 Spex 1459, "Uvisir" illuminator/sample chamber accessory
 SSR Instruments model 1208 polychromator
 Burleigh RC110, 5-pass, Fabry-Perot interferometer system
 - DAS-10 stabilization control electronics.
 Nicolet FTIR spectrometer
 FTIR spectrometer (Physics)
 Balzers QMG311 quadrupole mass spectrometer
 Perkin-Elmer 1-9 (V.A. Hospital)
 Perkin-Elmer 1-9 (Biology building)

Fluorometers

Model F2221 0.22m Computer-Controlled Spectrometer/Fluorolog
 - 450 W Xenon Lamp
 - Double-Grating Excitation and Emission Monochromators
 - Double-Beam Sample Compartment
 - Variable Slits
 - Nitrogen-Cooled Signal Detector
 Perkin-Elmer Fluorometer (V.A. Hospital)
 Perkin-Elmer Fluorometer (Biology building)

Power/Energy Radiometers

Coherent 210 Analog Power Meters
 IL1700 Research Radiometers
 International Light Power Meter for microwatt power measurements
 Laser Precision Model RT-20 Analog Thermopile Power Meters
 Laser Precision Model Rk-5000 Digital Power Meter/Radiometer
 Molelectron Pyroelectric Joulemeters
 Molelectron Model J3-02DW Joulemeter for Pulsed Nitrogen Laser
 Scientech Model 362 Analog Power/Energy Meter
 Scientech Model 365 Digital Power/Energy Meter
 Spectra-Physics 401C Power Meter
 United Detector Technology Digital Power Meters

Detection Systems

Array Detectors

CCD; Photometrics Ltd. Series 200 Camera System
 - Photometrics Model CC200 Camera Controller
 - Photometrics Model CE200 Temperature Control Unit
 - 512 x 512 Pixel Tektronix Back-thinned Array
 - Liquid Nitrogen Cooled.

SSR Instruments Model 1205A Self-Scanning Vidicon

High Speed Detector

Imacon 500 Series Streak Camera
 - single-shot mode, fast streak (20 ps to 5 ns)
 - single-shot mode, slow streak (1 ns to 100 ms)
 - synchroscan mode via modelocker or transducer synchronizing
 - Frequency range: 68-174 MHz
 - Scan speeds: 25 ps/mm
 - Resolution: 2 ps/mm
 - 2D image analysis system.

IR Detectors

Northcoast EO 817L germanium photodetector (800nm < λ < 1.8mm)
IR Associates PbS photoconductor (1mm < λ < 3.5mm)
IR Associates InSb photoconductor (3mm < λ < 5.5mm)
IR Associates HgCdTe photoconductor (5mm < λ < 14mm)

Silicon Detectors

EG&G Reticon HAD-1100A Silicon Photodiode (400nm < λ < 1.1mm)
Antel 35 picosecond rise-time Silicon Photodiode (400nm < λ < 1.1mm)
In-house 10MHz Silicon PIN Photodiode (400 nm < λ < 1.1mm)

Photomultipliers

RCA C31034 GaAs Photomultiplier Tubes (4)
Products for Research Photomultiplier Tubes (2)
Hamamatsu R1104 S20 Photomultiplier Tube (300nm < λ < 800nm)

Vacuum and Cryogenic Equipment

Diffusion Pumps

Varian Vacuum Ionization Gauge and Controller
Edwards Diffstak Diffusion Pump
Key Products Diffusion/Roughing Pump Evacuation System (10⁻⁷ torr)

Cryogenic

Air Products 1R04W SL Helium-Cooled Cryogenic Refrigeration System (10 Kelvin)
- Air Products Digital Temperature Control Accessory

Optical Equipment

Optical Tables (13)

Lenses

Fourier Transform Lenses (6)
Types: singlets, doublets, triplets, multiplets
Materials: glass, quartz, sapphire, ZnF₂, ZnSe, BaF₂, Ge
IR Lenses: NaCl, 400nm < λ < 14mm

Flat mirrors: Al, Au, Ag

Parabolic/spherical mirrors: Al, Ag, 600nm < λ < 60mm

Filters / Mounts / Stages

Electronics and General Lab Equipment

Arc Lamps / Light Sources

Oriel Tungsten Lamp (100W)
Oriel Tungsten-Halogen broadband temperature radiator (100-1000W)
Oriel Xenon Arc Lamp (100W)
Dolan-Jenner Model 190 Fiber Optic Illuminator

Cooling Systems (non-Cryogenic)

Nes-Lab Electro-Optic Model CFT-33 Refrigerated Recirculators (2)

Data Acquisition & Control (DAC)

International DAC Unit
Spectrometer DAC Units (2)
Mac Model 488A Bus Controller

Displays and Plotters

Electrohome CCD Display Monitor
Hewlett-Packard Model 1331A X-Y Display
Hewlett-Packard Model 7046B X-Y Flatbed Plotter

Omnigraphic X-Y Plotter

OmniScribe Strip-Chart Recorder

Watanabe Servocorder Model SR6312 Strip-Chart Recorder

Light Choppers

Sanford Research Model SR540, 4 KHz Mechanical Choppers (2)

Ortec 9479 Mechanical Chopper

Lock-in Amplifiers

Stanford Research Model SR510 Phase Sensitive Lock-in

Amplifiers (3)

Princeton Applied Research Model 5202 50MHz Lock-in Amplifier

Microscopes

Wild Model 327615 Microscope

Metalurgical Microscope

Unitron Me-No. 1340 Microscope

Modulators

Isomet 10MHz Acousto-Optic Modulator

NRC Model 845 Digital Shutter Controller

Oscilloscopes

Tektronix 2467, 400 MHz Dual-channel Oscilloscope

Tektronix 7904A "Fast" Oscilloscope

Tektronix 531A Oscilloscope

Tektronix 7623 Oscilloscope

Hewlett-Packard 1710A Oscilloscope

Photon Counters

Stanford Research Systems SR400 Two-Channel Gated Photon Counter

Princeton Applied Research Model 1109 Photon Counter

Special Electronic and Optical Equipment

Electronic equipment associated with picosecond time-domain

Optronic Laboratories Model 65 Precision Current Source (meter calibration)

Picosecond electronic equipment for pump & probe

Waretex 20MHz Signal Generator

General Misc. Lab Equipment

Laser dye mixer

Power supplies

Microgram scales

Function generators

Centrifuge

Digital/Analog multimeters

Tensiometer

Frequency counters

COMPUTER RESOURCES

Laser Institute Research Computer Network

- Apple Macintosh IIX Computer
 - 8 MB RAM / 160+80 MB hard disk
 - Color monitor
 - Auxiliary monitor
- Apple Macintosh II Computer
 - 8 MB RAM / 40 MB hard disk
 - Color monitor
- Apple Macintosh SE Computers w/hard disk (3)
- Apple Macintosh MacPlus computers w/hard disk (5)
- AppleTalk network
- Apple LaserWriter printer
- Apple ImageWriter printers (2)
- Modems - 1200 baud (3)
- CMS 60 MB Cassette-Tape Backup Unit
- Apple Scanner
- Apple II Computer with Metrabyte A/D board
- IBM Personal computers (3)
- IBM and Epson printers (3 total)
- Hewlett Packard terminal
 - for access to other computer networks.

IBM 3090/600S Super Computer (Super Computing Center)

- 6 vector processors
- Direct RAM: 256 megabytes
- Extended Mem: 2 gigabytes
- Disk Storage: 40 gigabytes
- Clock Rate: 15 ns
- ECL logic and 64 channels with graphics processing capabilities.
- Benchmarks: 798 megaflops/518 megaflops in 1000 x 1000 bench mark

ADDITIONAL FACILITIES AND CAPABILITIES

Animal / Biology Facilities

- Animal Clinic (V.A. Hospital)
 - Fully equipped animal laboratory facility.
- Animal Surgery Suite (Research Park)
 - Photodynamic Therapy
 - Laser Angioplasty
 - Laser Arterial Welding
- Cellular Biology Laboratories (V.A. Hospital)
 - Fully equipped facility.

Machine Shops - Several fully equipped shops.

Electronic Shops - Several fully equipped.

Materials Characterization Facilities